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We know you have choices where you take your education. On behalf of the entire Vision Expo event, we sincerely thank you for attending this session and being with us this year.
New Developments with OCT Testing in Glaucoma

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Disclosures

• Consultant – Alcon, Allergan, B & L, Carl Zeiss Meditec, Heidelberg Engineering, Inotek, Reichert, Topcon
New Developments with OCT

• Optic Nerve/RNFL/Posterior pole
  • What structure changes first as glaucoma develops?
  • Swept Source OCT
  • Confocal Scanning Laser Ophthalmoscopy
    • improved form of retinal photography
  • Advances in Optical Coherence Tomography
  • Flipping the TSNIT
  • Advances in digital imaging
Swept Source OCT

- Swept-source (SS) OCT is a next-generation OCT that demonstrates less signal decay over depth compared with the current SD OCT.
- Faster speed
- Probe light with a center wavelength of 1040 to 1060 nm, which allows high-penetration imaging deep retinal tissues such as Choroid and Sclera
- SS OCT improves visualization of the deep structures of the optic disc
- Compared with SD OCT, SS OCT is characterized by a higher speed scan rate and relatively lower sensitivity roll-off versus depth
- Would allow improved form of OCT Angiography
Swept Source OCT

• 100,000 A scans per second w 1 micron wavelength lightsource (1050 nm)
• Deep Tissue Imaging  
  • Penetrates deeper into retina for choroid and lamina assessment
• Images through cataracts
• Swept source OCT is faster because:
  • No spectrometer  
  • No line-scan camera (for detector)  
  • Utilizes tunable laser source  
  • ‘Sweeps’ across spectrum rapidly  
  • Photodiode detector (near instantaneous)
Clinically Is Change Seen First in the Optic Nerve or RNFL or Macula Area?

• The Heidelberg Retinal Tomography (HRT) may have been the best tool to detect early loss with the change in the optic disc
  • This device no longer available in the US
  • Normative database never fully developed
  • Its Topographic Change Analysis (TCA) was ahead of its time

• Until we have one scan that incorporates scanning all regions automatically, which scan do we use?
What is the OCT floor effect?

• The RNFL layer is composed of glial and other structural tissue
  • 40% of its makeup
• With advancing damage, never goes to 0
• The floor varies with OCT device but is between 50-60 um
Residual and Dynamic Range of Retinal Nerve Fiber Layer Thickness in Glaucoma: Comparison of Three OCT Platforms

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Purpose. To estimate visual field (VF) sensitivity at which retinal nerve fiber layer (RNFL) thinning reaches the measurement floor and at which RNFL stops thinning (change points), the dynamic range of RNFL thickness, and the number of steps from normal to RNFL floor among three optical coherence tomography (OCT) devices.

Methods. Glaucomatous patients (n = 58) and healthy subjects (n = 55-60) prospectively underwent VF testing and RNFL thickness measurement with Cirrus, Spectralis, and RTVue. Change points and corresponding RNFL thicknesses were estimated with simple linear regression (SLR) and Bayesian change point (BCP) analyses. The dynamic range and number of steps to RNFL floor were determined.

Results. The average VF change points and corresponding residual thickness at the time RNFL stopped thinning were −22.2 dB and 57.0 μm (Cirrus), −25.3 dB and 49.2 μm (Spectralis), and −24.6 dB and 64.7 μm (RTVue). The RNFL dynamic ranges derived from SLR values were wider on Spectralis (52.6 μm) than on Cirrus (35.4 μm) and RTVue (35.5 μm); the corresponding number of steps to reach the RNFL floor were 9.0 on Cirrus, 10.6 on Spectralis, and 8.3 on RTVue.

Conclusions. The relative VF sensitivity at which average RNFL thickness reaches the measurement floor, the residual layer thickness, and RNFL dynamic measurement range differ among the three devices. However, the number of steps from normal to the RNFL thickness floor is comparable.

Keywords: glaucoma, optical coherence tomography, retinal nerve fiber layer
Do You Wait For A Field Defect to Begin Therapy?
Retinal Ganglion Cell Count Estimates Associated with Early Development of Visual Field Defects in Glaucoma

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Purpose: To estimate retinal ganglion cell (RGC) losses associated with the earliest development of visual field defects in glaucoma.

Design: Observational cohort study.

Participants: The study group included 53 eyes of 53 patients with suspected glaucoma who were followed as part of the Diagnostic Innovations in Glaucoma (DIGS) study. These eyes had normal standard automated perimetry (SAP) visual fields at baseline and developed repeatable (3 consecutive) abnormal test results during a median follow-up of 6.7 years. An age-matched control group of 124 eyes of 124 healthy subjects recruited from the general population was included.

Methods: Estimates of RGC counts were obtained using a previously published model that combines estimates of RGC numbers from SAP sensitivity thresholds and retinal nerve fiber layer (RNFL) thickness measurements with spectral domain optical coherence tomography (SD-OCT). For eyes converting to glaucoma, estimates of RGC counts were obtained at the time (within ±3 months) of the first abnormal visual field, representing the time of earliest detection of visual field losses.

Main Outcome Measures: Estimates of RGC counts in eyes converting to glaucoma versus healthy eyes.

Results: The average RGC count estimate in the eyes with early visual field defects was 852,057 ± 115,829 cells, which was significantly lower than the average of 910,584 ± 142,412 cells found in healthy eyes (P < 0.001). Compared with the average number of RGCs in the healthy group, glaucomatous eyes had an average RGC loss of 28.4%, ranging from 6% to 57%, at the time of the earliest visual field defect on SAP. Retinal ganglion cell counts performed significantly better than the SD-OCT average RNFL thickness parameter in discriminating glaucomatous from healthy eyes with receiver operating characteristic curve areas of 0.95 ± 0.02 versus 0.88 ± 0.03, respectively (P = 0.001).

Conclusions: Glaucomatous eyes with the earliest detectable visual field loss on automated perimetry may already show substantial loss of RGCs. Empirical estimates of RGC counts combining structural and functional tests agreed closely with previous histologic reports on the number of RGCs associated with early visual field defects on SAP.
Macula Testing in Glaucoma

• Imaging to detect glaucoma damage has concentrated around RNFL and optic nerve evaluation

• Complicating the assessment of the optic nerve when evaluating for glaucoma damage is:
  • High variability of the ONH size and shape
    • Even among healthy individuals
  • Wide range of optic cup shapes and sizes
  • Variable size and configuration of blood vessels
  • Variable angle of penetration into the eyeball of the optic nerve (tilted disc)
  • Parapapillary changes such as atrophy

• These are the reasons why it is difficult to detect early glaucomatous damage
Flipping the RNFL

• TSNIT was an arbitrary designation 25 years ago
• Temporal region is most important part of curve and with NITSN, region is not broken up and loss more obvious
• Easier to recognize structure-function correlation
  • RNFL loss correlates easily with field loss
• Easier to understand if macula area may be involved and central field loss present
  • Is there a reduction in RNFL within the central $8^0$
On improving the use of OCT imaging for detecting glaucomatous damage

Donald C Hood, 1,2 Ali S Raza 1,3

ABSTRACT

Aims: To describe two approaches for improving the detection of glaucomatous damage using optical coherence tomography (OCT).

Methods: The two approaches described were: (a) a visual analysis of the high-quality OCT images and (b) a computer-aided detection algorithm based on a deep learning (DL) framework called傻DCT (semantic image segmentation with deep convolutional neural networks) that segments and classifies normal and abnormal retinal nerve fibre layer (RNFL) and ganglion cell complex (GCC) thicknesses. The傻DCT algorithm used two sets of training images, one to detect abnormal RNFL thickness and the other to detect GCC damage.

Results: A computer-aided analysis of the high-quality OCT images was feasible in patients with good image quality. The傻DCT algorithm correctly classified images with RNFL and GCC damage.

Conclusion: To improve the sensitivity and specificity of OCT imaging, high-quality OCT images should be assessed visually and computer-aided analysis can provide additional information about RNFL and GCC thicknesses.

INTRODUCTION

At one time, there was only one commercially available optical coherence tomography (OCT) machine and glaucoma specialists depended upon the summary report (figure 1A) based upon the most commonly used protocol. Numerous studies using this time-domain (TD) OCT machine found that the average retinal nerve fibre layer (RNFL) thickness (arrow 1), clock hour thickness (2), and quadrant thickness (3) provide good sensitivity and specificity for detecting glaucomatous damage (see reference 11). The傻DCT algorithm used two sets of training images, one to detect abnormal RNFL thickness and the other to detect GCC damage. The傻DCT algorithm correctly classified images with RNFL and GCC damage.

METHODS

The data from five eyes of five patients, with and without previous published studies, were used to illustrate this approach. All had glaucomatous optic neuropathy evaluated by OCT and all were part of a previously published study. 11,17

OCT protocol

A傻DCT machine (2D OCT-2000, Topcon) and the following three scan protocols were used: 6.0x6.0 mm HD disc (512 A-scans by 128 B-scans); 6.0x6.0 mm 3D macula (512 A-scans by 128 B-scans); and 3.4 mm disc circle (average of 50 scans; 1024 A-scans). The circle protocol involved...
RNFL - Two Methods for Display
What is EDI?
Enhanced Depth Imaging

• For spectral domain, sensitivity is highest at top of window (vitreous) and declines with depth

• With EDI, sensitivity in window is flipped and now sensitivity is higher on bottom (lamina or choroid)
  • Loss of sensitivity at top (vitreous)
  • Advantage of swept source is less drop off in sensitivity with depth of imaging

• Valuable to examine lamina cribosa visibility

• All OCTs have ability to shift sensitivity with depth
Enhanced Depth Imaging (EDI)

- Anterior surface of lamina cribrosa
- Posterior surface of lamina cribrosa
- Enhanced Depth Imaging (EDI)
- Bruch's membrane opening (Neural Canal Opening - NCO)
- Vitreous / Retinal interface highlighted
- Without EDI
- With EDI
- Posterior surface of lamina cribrosa
Optic Disc Analysis

• How Does An OCT Measure the Optic Disc Size?
  • What boundary is used for the disc edge?
    • Retinal pigment epithelial tips OR Bruch’s Membrane Opening (BMO)

• New parameter- Minimal Rim Width (MRW) to evaluate neuroretinal rim

• Both Cirrus and Spectralis use this metric

• Line drawn perpendicular from BMO to surface
Should the RNFL Ring Diameter be Greater than 3.5mm?
Glaucoma Diagnostic Capability of Circumpapillary Retinal Nerve Fiber Layer Thickness in Circle Scans With Different Diameters

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Purpose: To compare varying circumpapillary optical coherence tomographic (OCT) scan diameters for glaucoma diagnosis.

Materials and Methods: Prospective, cross-sectional, observational study. Circumpapillary retinal nerve fiber layer thickness (RNFLT) was measured using spectral-domain OCT in 1 randomly selected eye. Scans with diameters of 3.5, 4.1, and 4.7 mm were obtained, each with 7 parameters: mean global (G) RNFLT and mean RNFLT for the temporal-inferior (TI), nasal-inferior (NI), temporal-superior (TS), nasal-superior (NS), nasal (N), and temporal (T) sectors. Areas under the receiver operating characteristic curve (AUCs) were calculated.

Results: Mean age was 55 ± 18 years in 68 healthy eyes and 59 ± 15 years in 95 glaucomatous eyes (P = 0.12). Visual field mean deviation was −7.55 ± 6.61 dB in glaucomatous eyes. In all 3 circle scans, mean TI RNFLT had the greatest AUC (0.974 to 0.983), followed by mean G RNFLT (0.949 to 0.956). The AUC of mean TI RNFLT in the 4.1-mm scan (0.983) was greater than the AUCs of mean TI RNFLTs in the 4.7- (0.978; P = 0.128) and 3.5-mm (0.974; P = 0.049) scans. The AUC of mean TI RNFLT in the 4.1-mm scan (0.983) was greater than the AUCs of mean G RNFLTs in the 3.5- (0.954; P = 0.011), 4.1- (0.956; P = 0.016), and 4.7-mm (0.949; P = 0.011) scans. In 2 eyes with large parapapillary atrophy, RNFL segmentation error was noted only in the 3.5-mm scan in the area of parapapillary atrophy.

Conclusions: Further investigations to find the spectral-domain OCT circle scan diameter with the best diagnostic capability and the least artifacts are warranted, especially focusing on larger-than-conventional circle scans.

Key Words: glaucoma, imaging, optical coherence tomography, retinal nerve fiber layer

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A time-domain OCT circle scan with a diameter of 3.4 mm centered on the optic nerve head was reported to be more reproducible than scans with a diameter of 2.9 or 4.5 mm for RNFLT measurements. In addition to superior reproducibility, the authors also stated that the 3.4-mm circle scan is large enough compared with the 2.9-mm circle scan to avoid overlap with the optic disc but small enough compared with the 4.5-mm circle scan to allow RNFLT measurements in a thicker area. A circle scan diameter of \( \sim 3.4 \text{ mm} \) was shown to have good diagnostic capability for glaucoma in both time-domain and spectral-domain OCT devices. Most OCT instruments use a circle scan diameter of \( \sim 3.4 \text{ mm} \).

However, there is little work in the literature to demonstrate that the 3.4-mm circle is significantly better than others in discriminating between healthy and glaucomatous eyes. Larger diameter circles may theoretically sample RNFL areas that are less affected by blood vessel variation and irregularity because large blood vessels branch into more evenly distributed smaller vessels further from the optic disc. In addition, larger diameter circles may avoid areas of parapapillary atrophy, which result in RNFL segmentation errors. The purpose of this study is to compare the diagnostic capability of circumpapillary RNFLT for glaucoma among circle scans with different diameters.
### TABLE 2. RNFLT Values (μm) in Circle Scans With Different Diameters in Normal and Glaucomatous Eyes

<table>
<thead>
<tr>
<th></th>
<th>3.5-mm Circle Scan</th>
<th>4.1-mm Circle Scan</th>
<th>4.7-mm Circle Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Glaucoma</td>
<td>Normal</td>
</tr>
<tr>
<td>G</td>
<td>96.5 ± 12.3</td>
<td>64.3 ± 15.1</td>
<td>83.1 ± 9.8</td>
</tr>
<tr>
<td>TI</td>
<td>148.2 ± 21.1</td>
<td>75.4 ± 29.5</td>
<td>132.2 ± 17.8</td>
</tr>
<tr>
<td>NI</td>
<td>105.9 ± 24.2</td>
<td>68.2 ± 19.9</td>
<td>84.8 ± 19.0</td>
</tr>
<tr>
<td>TS</td>
<td>130.7 ± 22.6</td>
<td>81.5 ± 29.9</td>
<td>118.3 ± 18.4</td>
</tr>
<tr>
<td>NS</td>
<td>111.6 ± 23.4</td>
<td>77.7 ± 24.6</td>
<td>90.4 ± 18.9</td>
</tr>
<tr>
<td>N</td>
<td>77.1 ± 14.6</td>
<td>56.6 ± 16.4</td>
<td>64.9 ± 11.2</td>
</tr>
<tr>
<td>T</td>
<td>71.5 ± 11.7</td>
<td>53.8 ± 17.1</td>
<td>64.3 ± 9.9</td>
</tr>
</tbody>
</table>

G indicates global average; N, nasal; NI, nasal-inferior; NS, nasal-superior; RNFLT, retinal nerve fiber layer thickness; T, temporal; TI, temporal-inferior; TS, temporal-superior.

All P-values were < 0.001 when comparing retinal nerve fiber layer thickness between normal and glaucomatous eyes for all 7 parameters in all 3 circle scans.

### TABLE 4. Area Under the Receiver Operating Characteristic Curves of RNFLT Parameters in Circle Scans With Different Diameters (Mild to Moderate Glaucoma)

<table>
<thead>
<tr>
<th>RNFLT</th>
<th>3.5-mm Circle Scan*</th>
<th>4.1-mm Circle Scan*</th>
<th>4.7-mm Circle Scan*</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>0.941 (0.888-0.973)†</td>
<td>0.944 (0.892-0.976)†</td>
<td>0.941 (0.888-0.973)†</td>
<td>0.512</td>
<td>1.000</td>
<td>0.611</td>
</tr>
<tr>
<td>TI</td>
<td>0.967 (0.922-0.990)†</td>
<td>0.978 (0.939-0.995)†</td>
<td>0.972 (0.930-0.993)†</td>
<td>0.060</td>
<td>0.486</td>
<td>0.177</td>
</tr>
<tr>
<td>NI</td>
<td>0.866 (0.798-0.917)</td>
<td>0.854 (0.785-0.908)</td>
<td>0.823 (0.750-0.882)</td>
<td>0.332</td>
<td>0.027</td>
<td>0.071</td>
</tr>
<tr>
<td>TS</td>
<td>0.861 (0.792-0.913)</td>
<td>0.876 (0.810-0.925)</td>
<td>0.883 (0.818-0.931)</td>
<td>0.214</td>
<td>0.122</td>
<td>0.437</td>
</tr>
<tr>
<td>NS</td>
<td>0.811 (0.737-0.872)</td>
<td>0.796 (0.720-0.860)</td>
<td>0.795 (0.718-0.858)</td>
<td>0.350</td>
<td>0.320</td>
<td>0.871</td>
</tr>
<tr>
<td>N</td>
<td>0.793 (0.717-0.857)</td>
<td>0.811 (0.737-0.872)</td>
<td>0.806 (0.731-0.867)</td>
<td>0.114</td>
<td>0.454</td>
<td>0.587</td>
</tr>
<tr>
<td>T</td>
<td>0.732 (0.651-0.803)</td>
<td>0.723 (0.641-0.795)</td>
<td>0.735 (0.654-0.806)</td>
<td>0.518</td>
<td>0.868</td>
<td>0.377</td>
</tr>
</tbody>
</table>

Boldface type indicates statistical significance defined as P < 0.05.

* AUC (95% confidence interval).

†A significantly greater AUC than the AUCs of mean T, TS, N, NS, and NI RNFLT thickness within the same circle scan (all P < 0.05).

AUC indicates area under the receiver operating characteristic curve; G, global average; N, nasal; NI, nasal-inferior; NS, nasal-superior; RNFLT, retinal nerve fiber layer thickness; T, temporal; TI, temporal-inferior; TS, temporal-superior.

P1 = P-value between 3.5- and 4.1-mm scans; P2 = P-value between 3.5- and 4.7-mm scans; P3 = P-value between 4.1- and 4.7-mm scans.
FIGURE 2. Receiver operating characteristic curves for mean temporal-inferior (TI) and mean global (G) retinal nerve fiber layer thickness (RNFLT) in 3 circle scans (3.5, 4.1, and 4.7 mm diameters) to distinguish glaucomatous from normal eyes. The mean TI RNFLT in the 4.1-mm circle scan has the greatest area under the receiver operating characteristic curve.
Combined Reports
More Importantly, Use Neural Networks and Other Advanced Statistical Methods to Recognize Early Loss Using Information from Both Structural and Functional Tests
Measuring Blood Flow

• Ocular blood flow and optic nerve injury have been linked
• The question still not answered is which comes first
• Can a device be developed that provides reproducible, quantitative, objective assessment of retinal and optic nerve blood flow
  • Both global and local
  • Does not require expert operator
  • Measurement should correlate with structure and function
Measuring Blood Flow

• There have been numerous devices to measure blood flow over the years
  • Varying degrees of invasiveness, accuracy and precision
    • From injectable dyes to ultrasonography to laser
    • Poorly reproducible or variations in acquisition of data

• Optical Coherence Tomography Angiography
  • Used to map retinal and superficial optic nerve vasculature and blood flow
  • Not clear if there is a floor effect
  • Is technique useful from early to advanced disease?
OCT - Angiography

• Retinal vascular imaging technology that uses a novel algorithm to generate high resolution images and quantify vessel density and blood flow of the retina and choroid
  • Vessel density changes in OAG have been demonstrated with OCT-A
  • No dye, not invasive
  • Short scan time
  • Three-dimensional imaging
  • Specifically analyses the posterior retinal and choroidal microvasculature
  • If the results indicate a loss of vessel density, one cannot differentiate the etiology between tissue (capillary) loss and acute ischemia

• Fluorescein angiography (FA) is used to visualize the superficial retinal vascular beds and extravasation of vascular fluid secondary to retinal pathology
  • Invasive requiring dye injection
  • Lacks depth information
OCT-A

• Limitations
  • Patient movement can reduce the quality of the OCT-A image
  • Patient must have very good fixation, requiring the patient to remain still and avoid blinking during the examination
  • In addition, while the algorithm does improve the SNR compared with a full bandwidth variant, the resolution of the image is compromised
  • OCT-A with the SSADA algorithm has a resolution of 18 mm, rather than 5 mm for a full bandwidth algorithm
  • Finally, low amounts of blood flow near the defined threshold may be undetected
Future of Imaging

• Present structural and functional information together
  • Hood presentation
  • Allows earlier damage to be recognized
  • Use information from each to provide better diagnostic information

• Role of central fields in diagnosing and monitoring glaucoma
  • Incorporating fields with imaging

• Combined Reports
  • OCT/Photographs with Visual Fields